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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,292	01/27/2006	Nicoletta Almirante	026220-00073	1937
4372	7590	11/23/2009	EXAMINER	
ARENT FOX LLP 1050 CONNECTICUT AVENUE, N.W. SUITE 400 WASHINGTON, DC 20036			KOSACK, JOSEPH R	
			ART UNIT	PAPER NUMBER
			1626	
			NOTIFICATION DATE	DELIVERY MODE
			11/23/2009 ELECTRONIC	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DCIPDocket@arentfox.com  
IPMatters@arentfox.com  
Patent\_Mail@arentfox.com

### Office Action Summary

**Application No.**

10/566,292

**Applicant(s)**

ALMIRANTE ET AL.

**Examiner**

Joseph R. Kosack

**Art Unit**

1626

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 August 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-3 and 5-21 is/are pending in the application.
- 4a) Of the above claim(s) 3, 16, 17 and 19-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 5-15 and 18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB06)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 1-3 and 5-21 are pending in the instant application.

#### ***Previous Claim Rejections - 35 USC § 103***

Claims 1, 2, 5-15, and 18 were previously rejected under 35 U.S.C. 103(a) as being unpatentable over McIntyre et al. (*Pharmacol. Ther.*, 1997, 181-194) in view of Del Soldato (WO 00/61537, referred to below as Del Soldato I) and Del Soldato (WO 95/09831, referred to below as Del Soldato II).

The Applicant has traversed the rejection on the grounds that the use of losartan combined with the Del Soldato references would not yield the instant invention, that Del Soldato II does not teach the specific linker, nor does Del Soldato II teach the attachment to an angiotensin II receptor blocker, and that the instant compounds show superior properties.

The Examiner respectfully disagrees. Firstly, Del Soldato I is the reference which teaches the nitrooxy tether of the instantly elected species, not Del Soldato II. The purpose of Del Soldato II is to show that the nitrooxy tether can be attached directly to the drug and not through an anti-oxidant moiety. Additionally, the person of ordinary skill would be motivated to look to Del Soldato II as both Del Soldato references are drawn to drugs with nitrooxy tethers in order to reduce side effects due to oxidative stress and to the elderly. Del Soldato I specifically mentions losartan as a drug capable to be modified in this way. Even though the instant compounds may have improved effectiveness compared to the base drug, losartan, the case for obviousness is stronger than the superior properties demonstrated as other improvements were expected by the

Del Soldato references such as reduced side effects. Therefore, the Applicant's arguments have been considered fully, but were not found to be persuasive by the Examiner. The rejection is maintained.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 5-15, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over McIntyre et al. (*Pharmacol. Ther.*, 1997, 181-194) in view of Del Soldato (WO 00/61537, referred to below as Del Soldato I) and Del Soldato (WO 95/09831, referred to below as Del Soldato II).

The instant claims are drawn to nitrooxy derivatives of Angiotensin II receptor blocker drugs. The species searched is a derivative of the drug losartan.

McIntyre et al. teach the drug losartan. See the whole document, specifically page 182 for the structure of losartan.

McIntyre et al. do not teach attaching a nitrooxy tether to the drug as instantly claimed.

Del Soldato I teaches that the addition of a nitrooxy tether to drugs such as losartan remove side effects to patients affected by oxidative stress and/or endothelial dysfunctions or to the elderly in general. See pages 6-13. The exact tether that is used in the elected species is shown in Example 10 on page 84, albeit attached to a bridging component.

Del Soldato II teaches that a nitrooxy tether can be attached directly to a drug such as naproxen. See page 14, line 20 through page 16, line 17.

Therefore, on of ordinary skill in the art would be motivated to take losartan, which is discussed at length by McIntyre et al. and attach the nitrooxy tether as shown by Del Soldato I described as capable of function with losartan, and directly to the drug as taught in Del Soldato II, with a reasonable expectation of success. The motivation for making the change is that the addition of a nitrooxy tether to drugs such as losartan

remove side effects to patients affected by oxidative stress and/or endothelial dysfunctions, or to the elderly in general.

Thus, the claims are *prima facie* obvious over the prior art.

### ***Conclusion***

Claims 1, 2, 5-15, and 18 are rejected.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph R. Kosack whose telephone number is (571)272-5575. The examiner can normally be reached on M-Th 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Joseph R Kosack/  
Examiner, Art Unit 1626